PATENT & TRADEMARK OFFICE
AUG 0 2 2004
OIPE

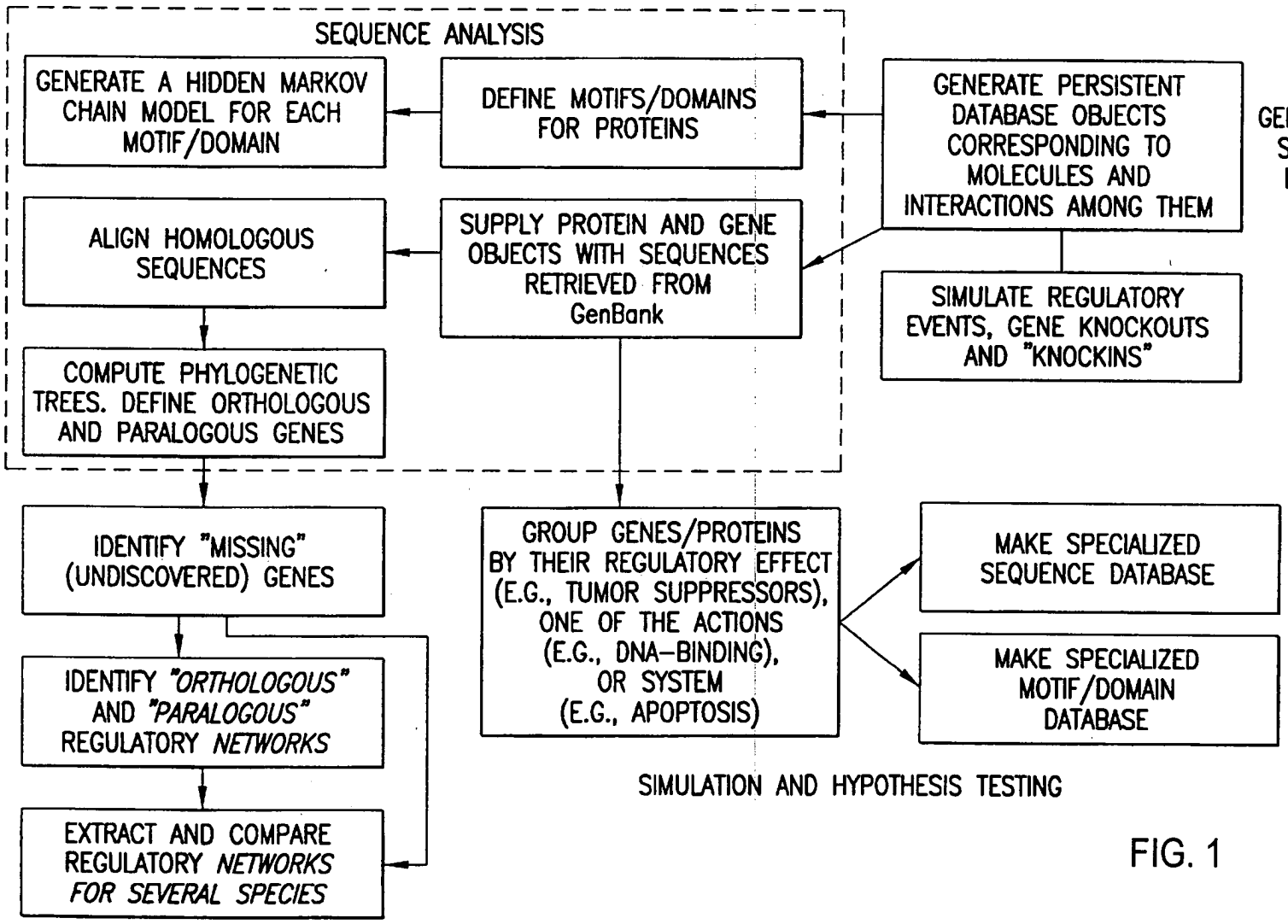

FIG. 1

O I P E
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PATENT & TRADEMARK OFFICE

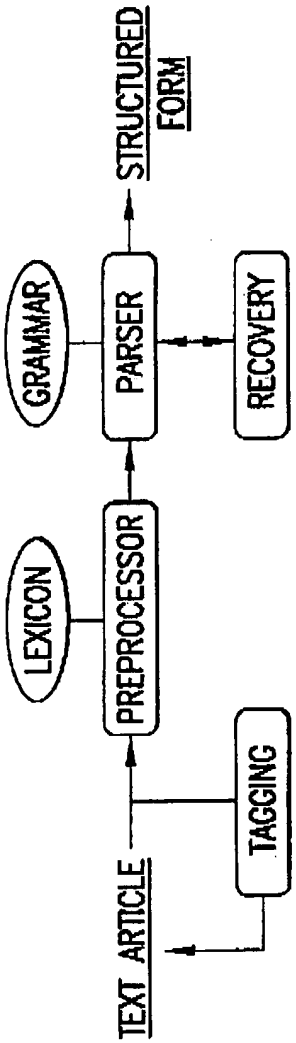

FIG. 2

PATENT & TRADEMARK OFFICE
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OIPE

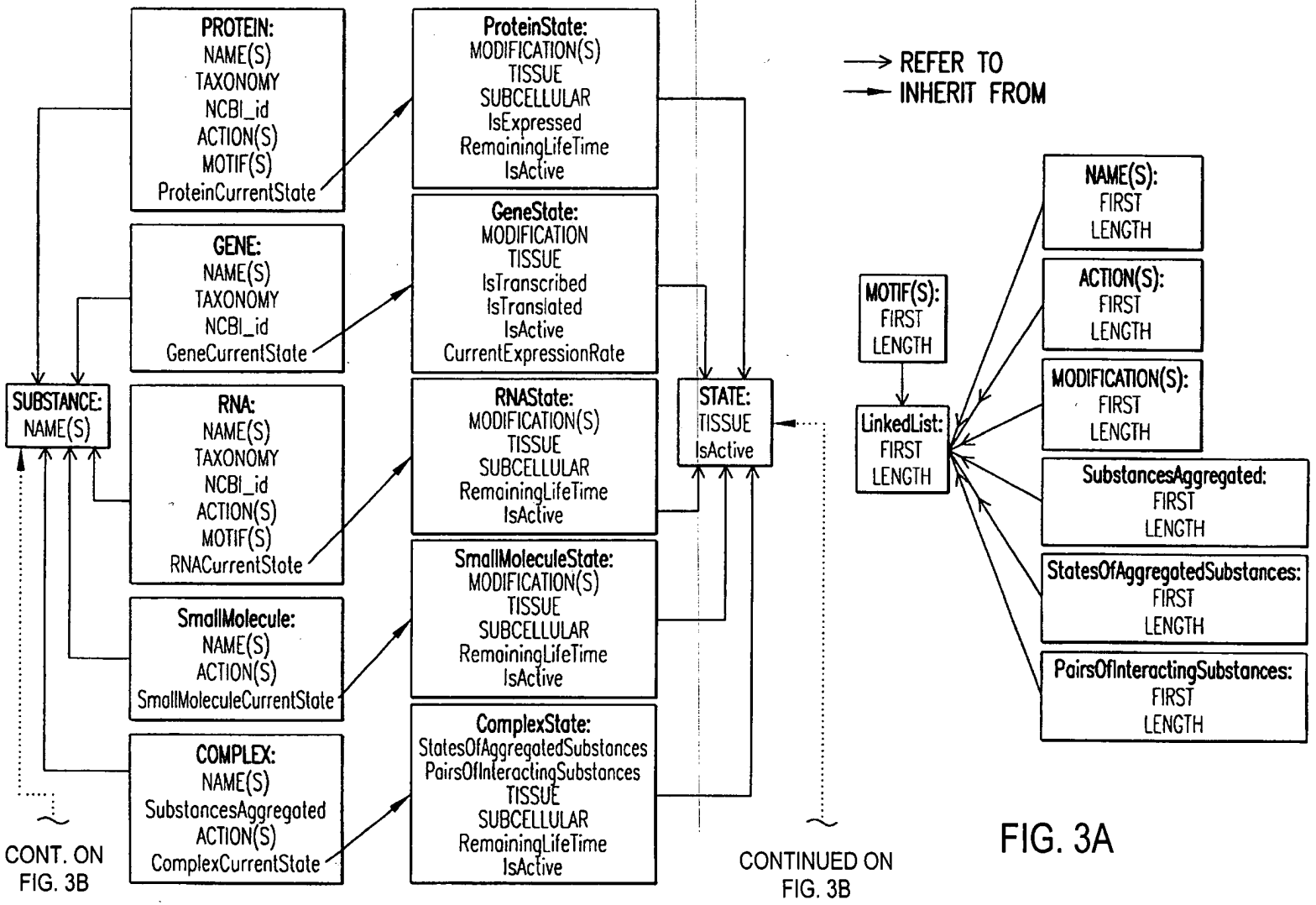

FIG. 3A

PATENT & TRADEMARK OFFICE
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OIPE
JC11

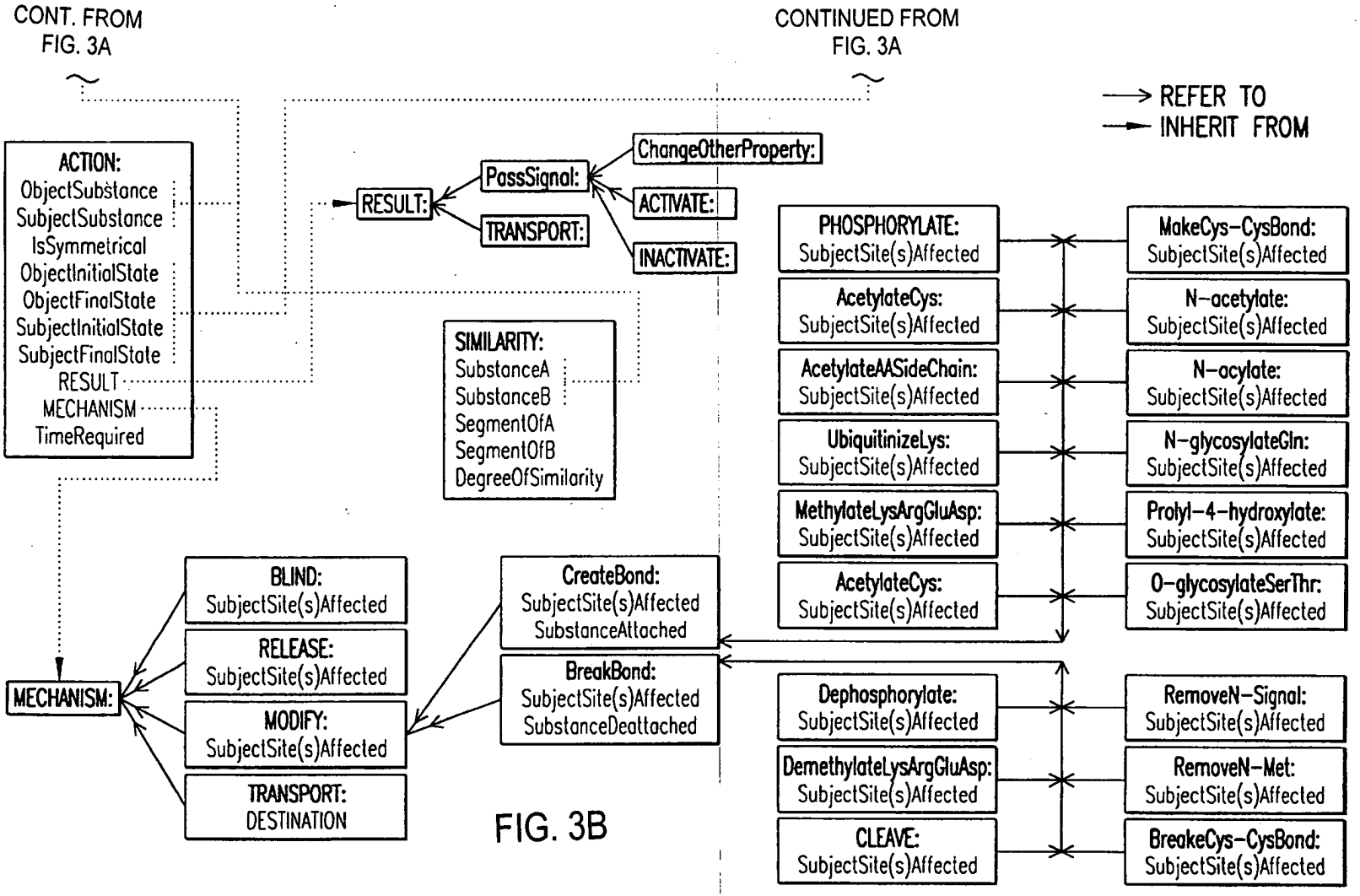

FIG. 3B

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bci-xL / bci / bci-xS / ced-9 / Bax / Blk / Bak / p21 / NGFI-B / N10 /Nak1 / Nur77 / Nurr 1 / Nor-1 / Noi-1 / RXR/ galectin-1 / N-glycan / CNTF / lck / fyn / ZAP-70 / raf / ras / MAP / protein kinase C / PKC / phosphatase calcineurin / NF-AT / AP1 / 14-3-3 / Raf-1 / Bci-2 / interieukin / IL-1 / IL-3 / cytokine / IGF-1 / CD95 / Apo-1 / RIP / FAF1 / FADD / FAP-1 / TNFR / TRAF / TRAP1 / TRAP2 / TRADD / H1AP1 / H1AP2 / CD40 / CD30 / X1AP / CD2 / CD3 / TCR / Bci-w / Mci-1 / NR-13 / BHRF1 / HMW5-HL / E1B19K / Nbk / Mch2 / CPP32 / ICE / FLICE / Nedd-2 / TX / Mch3 / Mch4 / ICB-1s / nor-1 / DNAseI / caspase / MACH1 / Mch5 / apopain / Yama / ICH / CMH / ced-3 / ced-4 / ced-9 / p53 / MKK3 / MKK1 / MKK2 / MKK4 / BAG-1 / Src / FAST/ p38 / p42 / ERK1 / p44 / ERK2 / SAPK / JNK / MEK / C-JUN / MEF2D / ATF2 / calcineurin / ELK-1 / protein phosphatase 2A / raf-1 / IL-I beta / TNF / PTK / Apaf / p35 / ETS / C-Myc / IL-2 / IL-2 receptor / NF-kappa B / TNFR-1 / TRAIL / APO-2L / DR4 / death receptor / DR3 / DR2 / DR5 / DR1 / bod / BMPR / BMP-x / TGF / grim / bid / FAN / perforin / Fas-L / Fas / DcR1 / decoy receptor / wxi-1 / NGF receptor / growth factor / RAR

FIG. 4

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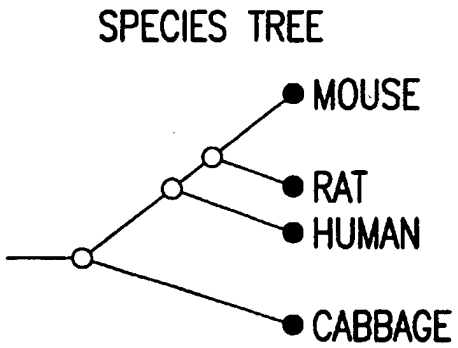
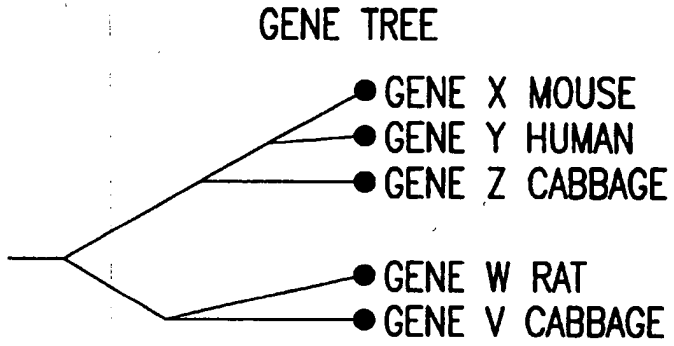
OIPE





○DUPLICATION DUE TO SPECIATION
⊘INTRAGENOME DUPLICATION
●PRESENT-DAY GENES

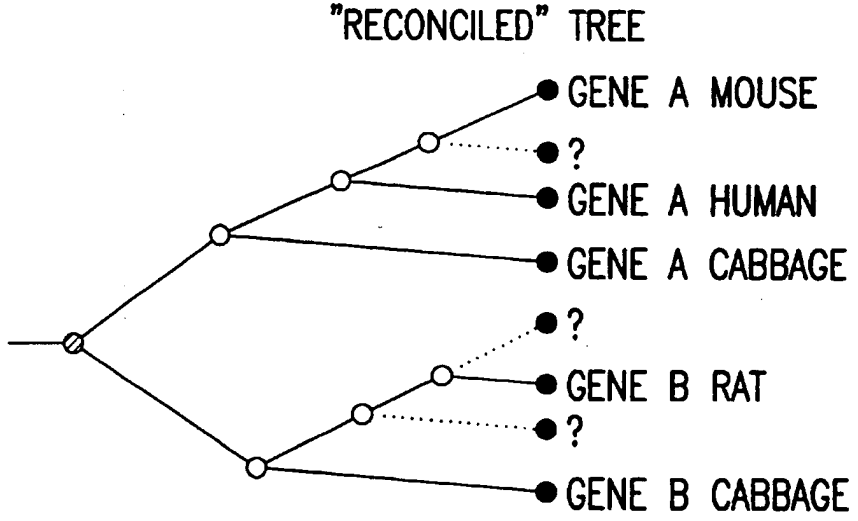
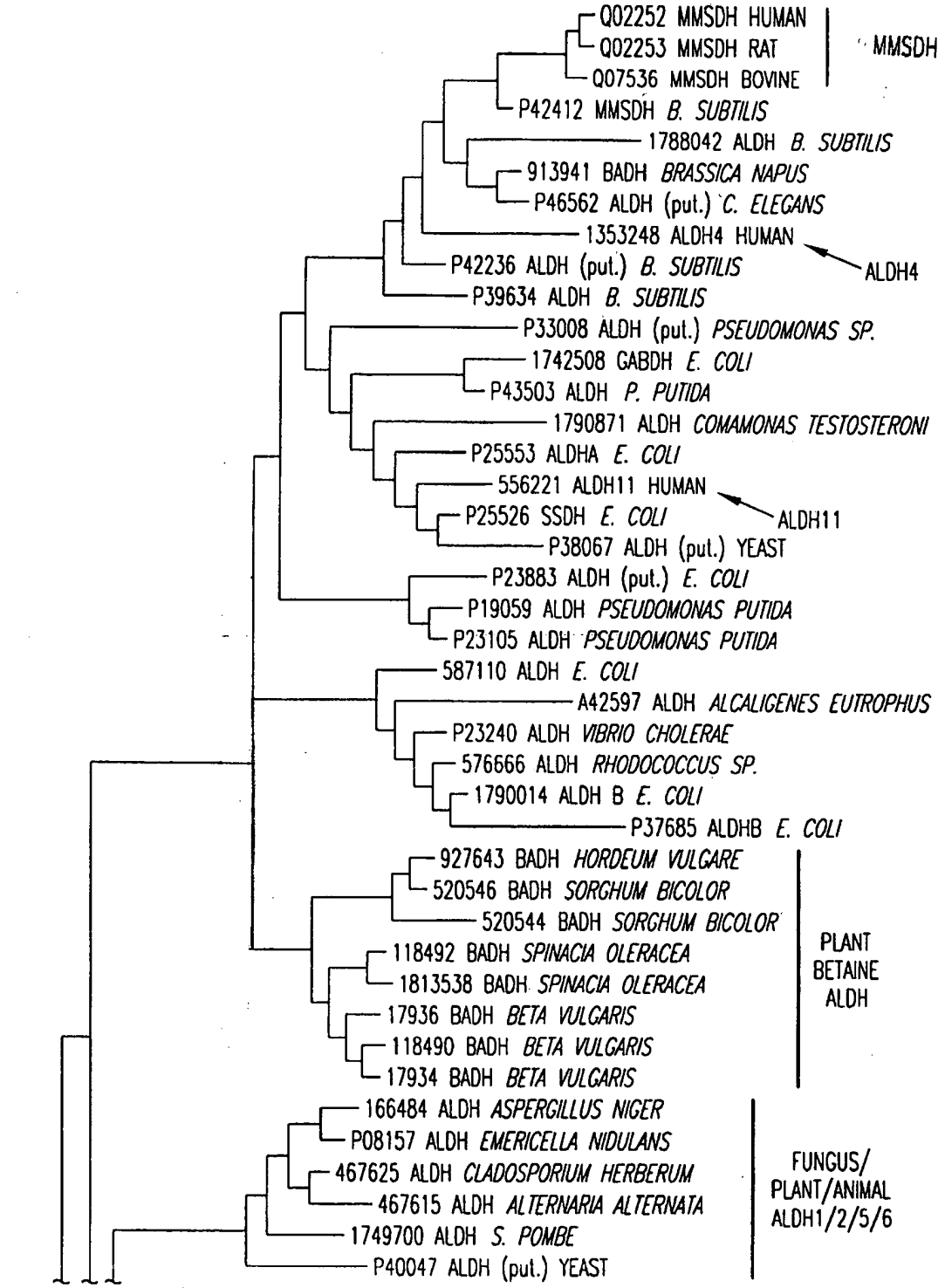


FIG. 5

OIPE
AUG 0 2 2004
PATENT & TRADEMARK OFFICE



CONTINUED ON FIG. 6B

FIG. 6A

O I P E
AUG 0 2 2004
PATENT & TRADEMARK OFFICE

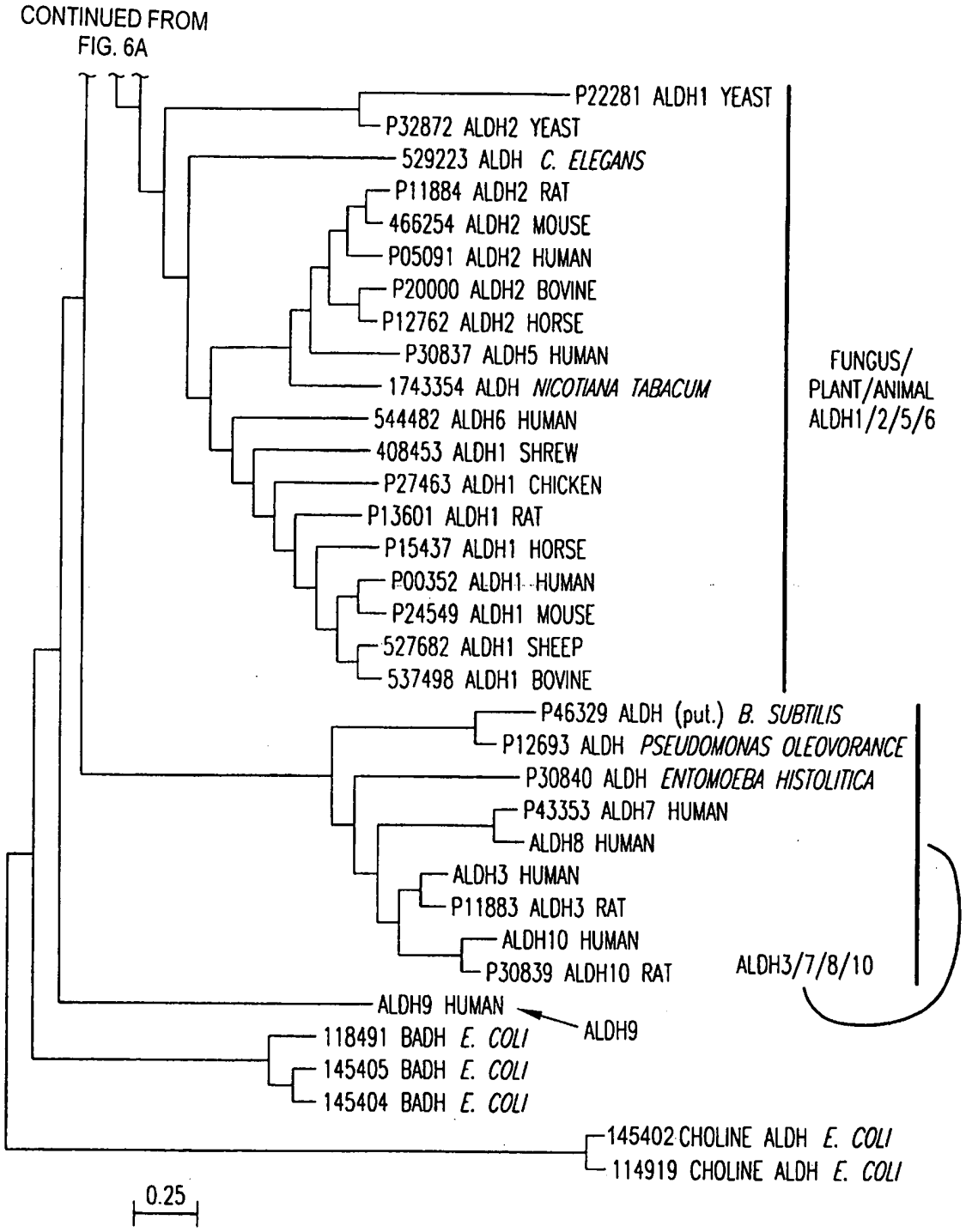
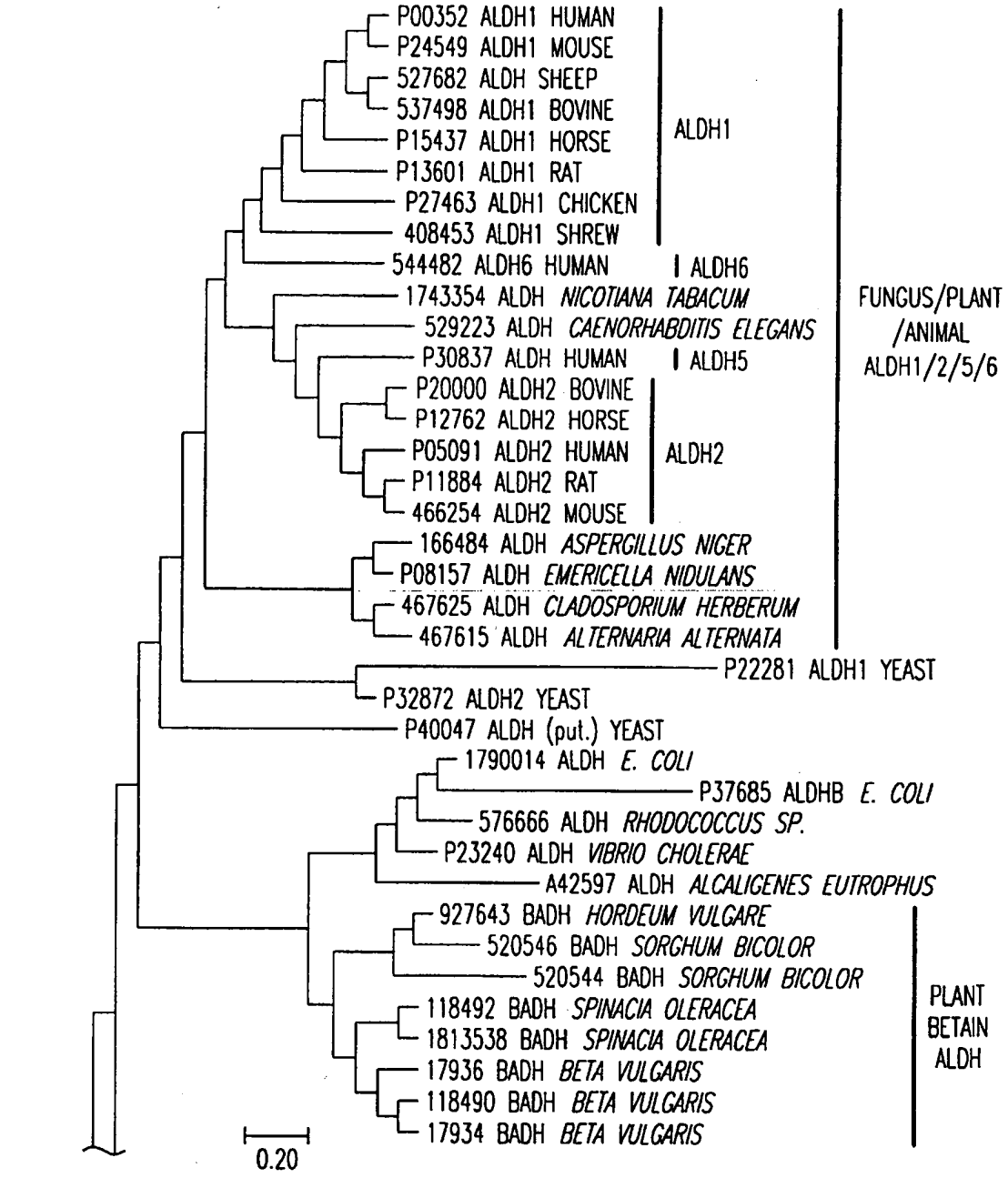


FIG. 6B

OIPE
AUG 0 2 2004
PATENT & TRADEMARK OFFICE



CONTINUED ON
FIG. 7B

FIG. 7A

OIPE
AUG 0 2 2004
PATENT & TRADEMARK OFFICE

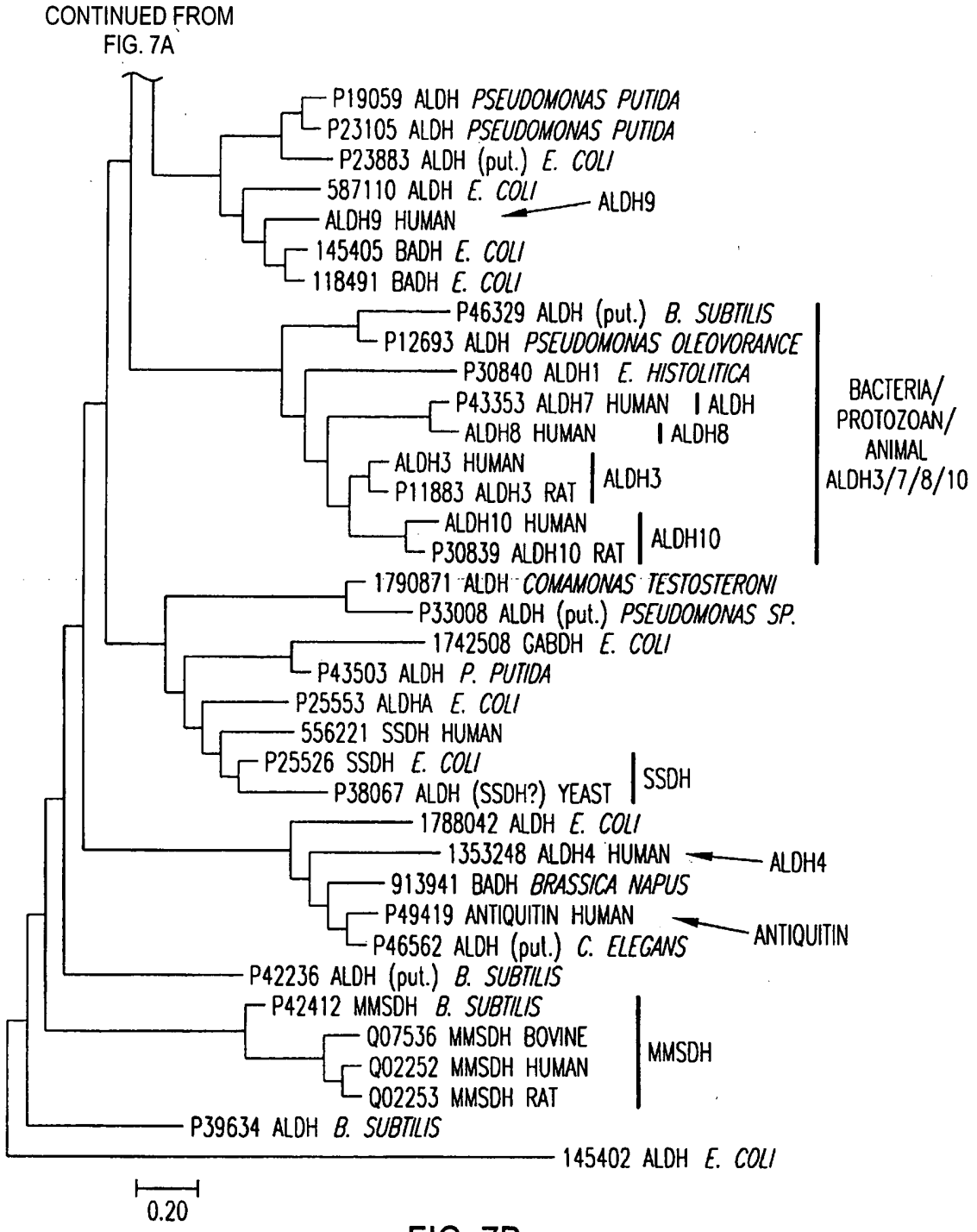


FIG. 7B

OIPE
AUG 0 2 2004
PATENT & TRADEMARK OFFICE

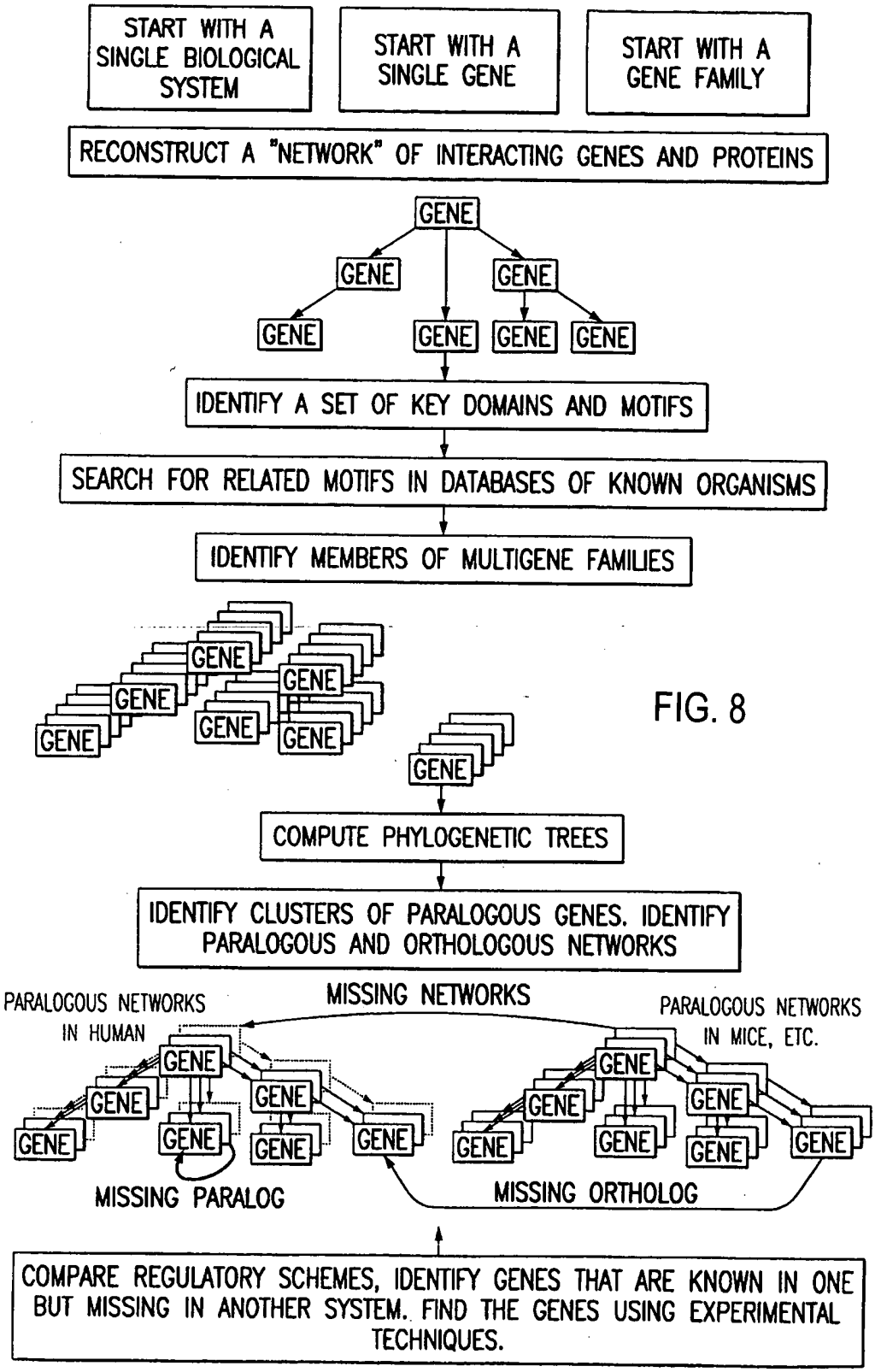


FIG. 8

OIPE
AUG 0 2 2004
PATENT & TRADEMARK OFFICE

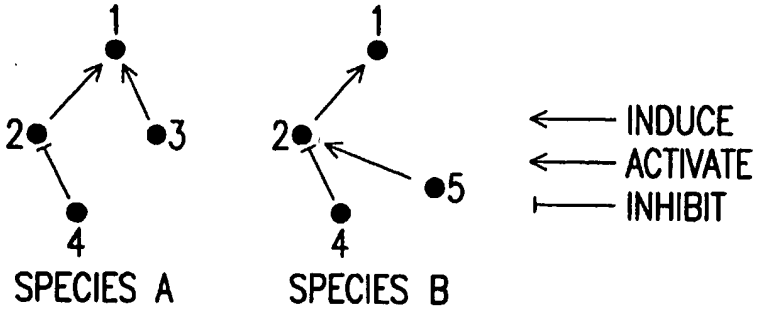


FIG. 9A

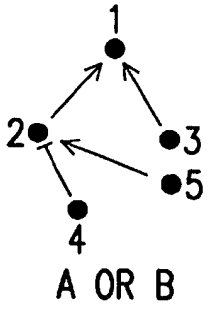


FIG. 9B

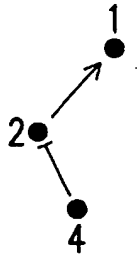


FIG. 9C

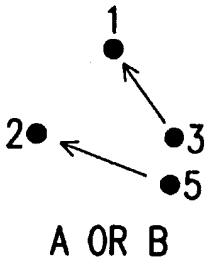


FIG. 9D

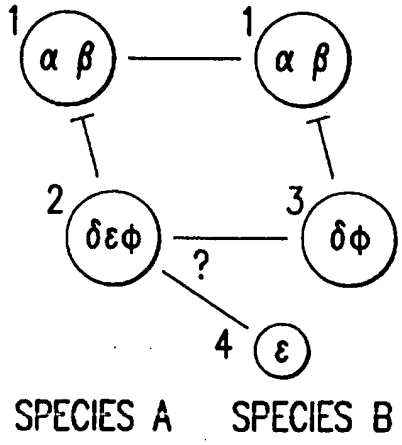


FIG. 10

OIPE
AUG 0 2 2004
PATENT & TRADEMARK OFFICE

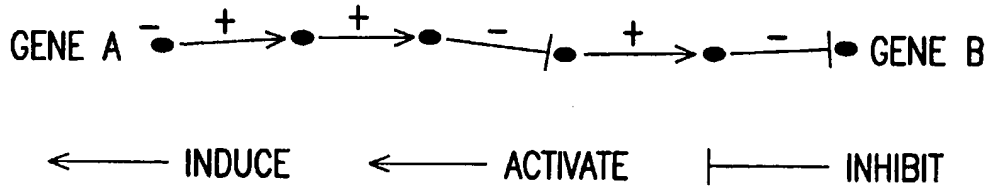


FIG. 11A

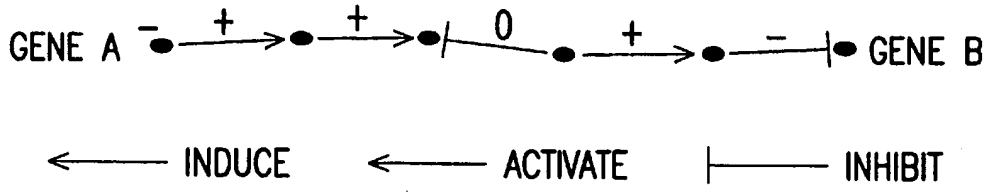


FIG. 11B

AUG 0 2 2004
PATENT & TRADEMARK OFFICE

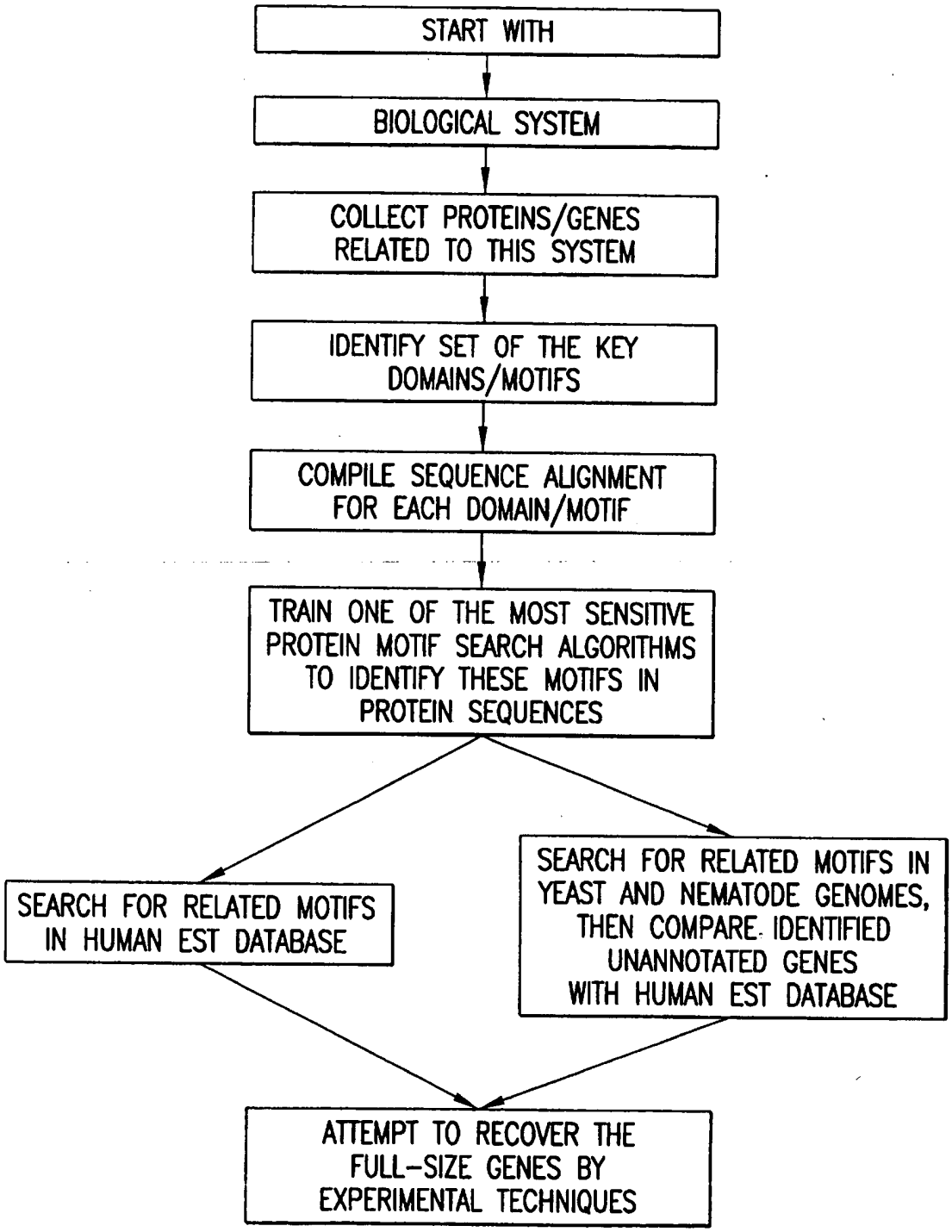


FIG. 12

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LEGEND FOR FIGS. 13A, 13B AND 13C

- POZ/BTB DOMAIN
- KELCH REPEAT
- RING FINGER DOMAIN
- FIBRONECTIN III DOMAIN
- CYCLIN REPEAT
- EGF-LIKE DOMAIN
- CUB DOMAIN
- LAMININ EGF-LIKE DOMAIN
- TRANSMEMBRANE HELIX
- BP-BIPARTITE NUCLEAR LOCALIZATION SIGNAL
- TRANSFERASE DOMAIN
- NEW A-DOMAIN
- NEW POZ-LINKER DOMAIN
- NEW B-DOMAIN
- NEW SPOP DOMAIN
- NEW (?) TN (TUMOR NECROSIS) DOMAIN
- FOS/JUN DNA-BINDING DOMAIN
- gi|1707204-DOMAIN
- NEW HAT DOMAIN (HEMAGGLUTININ, ALPHA TOXIN, TUMOR NECROSIS-FACTOR-ALPHA-INDUCED PROTEIN)
- DEATH DOMAIN
- KINASE DOMAIN
- HEAT REPEAT
- Zn-FINGER C_2H_2
- PROLINE-RICH REGION
- PKC-C1 DOMAIN, GAG/PE-BINDING
- PKC-C2 DOMAIN
- PROTEIN KINASE DOMAIN

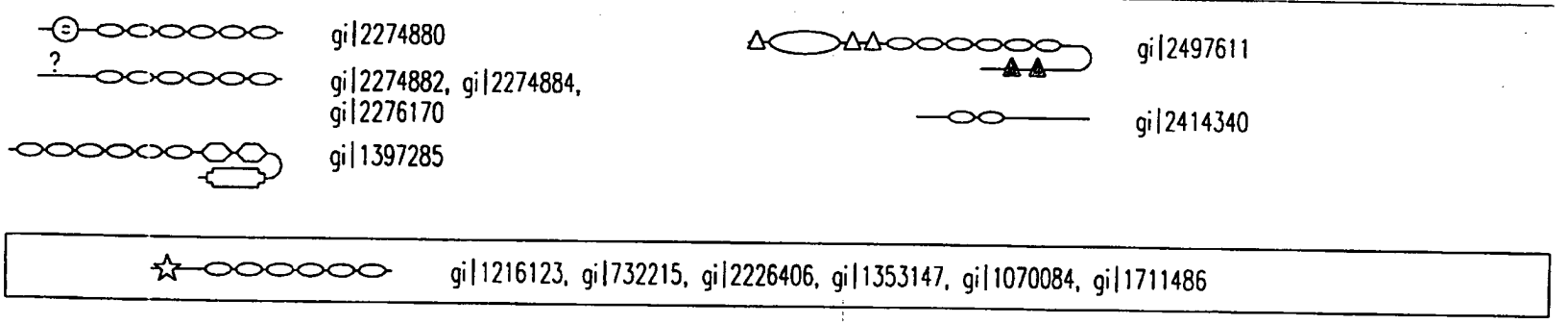
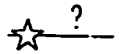
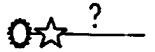


FIG. 13A

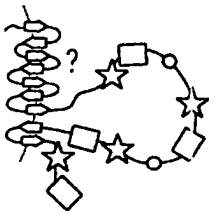
PATENT & TRADEMARK OFFICE
AUG 0 2 2004
JC11



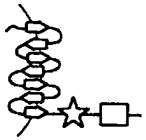
gi|1465836, gi|1707203, gi|2315752, gi|465779, gi|1707205, gi|2429493, gi|1707215, gi|1070062, gi|2315655



gi|2291257

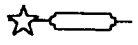


gi|2394485

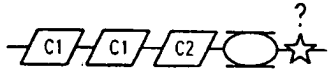


gi|1132514

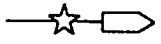
gi|529718, gi|1526968 (MEL26), gi|466032, gi|1176717



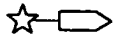
gi|1707217, gi|1707213, gi|1707214, gi|2315750, gi|2315635, gi|1707216, gi|2315748, gi|1707212, gi|1707202, gi|2315636, gi|2315655, gi|2315634, gi|2315541, gi|2315634



gi|868172



gi|2315751



gi|1707204, gi|1707206, gi|2315660, gi|2315661, gi|2315757 (POZ IS TRUNCATED)

gi|522131

FIG. 13B

PATENT & TRADEMARK OFFICE
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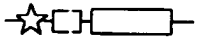
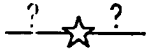
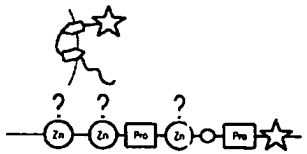
JC11



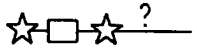
gi|2497016



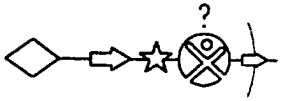
gi|1914354, gi|1293841, gi|1326360, gi|1326361 (B0496.2), gi|1065930, gi|2315541, gi|1049377, gi|1049378, gi|1132541, gi|1903102, gi|1122793, gi|1086886, gi|1729689, gi|1256456, gi|1438721, gi|1256451, gi|1429312



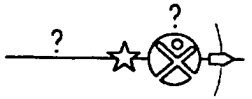
gi|2315652



gi|2315688

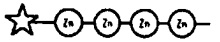


gi|1132541



gi|1469056

gi|2315570 (POZ IS TRUNCATED), gi|2315788, gi|2429424



gi|671825

FIG. 13C

PATENT & TRADEMARK OFFICE
AUG 0 2 2004
JC714

>gi|2210766|gb|AA481214|AA481214 aa34e02.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:815162 5' similar to WP:W07A12.4 CE03795 :, mRNA sequence [Homo sapiens]
CATGGCTTCCTGGACACCAACCCTGCCATCCGGGAGCAGACGGTCAAGTCCATGCTGCTCCTGGCCCCAA
AGCTGAACGAGGCCAACCTCAATGTGGAGCTGATGAAGCACTTTGCACGGCTACAGGCCAAGGATGAACA
GGGCCCCATCCGCTGCAACACCACAGTCTGCCTGGGCAAAATCGGCTCCTACCTCAGTGCTAGCACCAGA
CACAGGGTCCTTACCTCTGCCTTCAGCCGAGCCACTAGGGACCCGTTTGCACCGTCCCGGGTTGCGGGTG
TCCTGGGCTTTGCTGCCACCCACAACCTCTACTCAATGAACGACTGTGCCCAGAAGATCCTGCCTGTGCT
CTGCGGTCTCACTGTAGATCCTGAGAAATCCGTGCGAGACCAGGCCTTCAAGGCA ID8

>gi|1349211|gb|W51957|W51957 zc45f01.r1 Soares_senescent_fibroblasts_NbHSF Homo sapiens cDNA clone IMAGE:325273 5', mRNA sequence [Homo sapiens]
CCTTCGAGTTCGGCAATGCTGGGGCCGTTGTCCTCACGCCCCTCTTCAAGGTGGGCAAGTTCCTGAGCGC
TGAGGAGTATCAGCAGAAGATCATCCCTGTGGTGGTCAAGATGTTCTCATCCACTGACCGGGCCATGCGC
ATCCGNCTCCTGCAGCAGATGGAGCAGTTCATCCAGTACCTTGACGAGCCAACAGTCAACACCCAGATCT
TCCCCCACGTCGTACATGGCTTCCTGGACACCAACCCTGCCATCCGGGAGCAGACGGTCAAGTCCATGCT
GCTCCTGGCCCCAAAGCTGAACGAGGCCAACCTCAATGTGGAGCTGATGAAGCACTTTGCACGGCTACAG
GCCAAGGATGAACAGGGCCCCATCCGCTGCAACACCACAGTCTGCCTGGGCAAAATCGGCTCCTACCTCA
GTGCTAGCACCAGACACAGGGTCCTTACCTCTG ID9

FIG. 14A

OIPE
AUG 0 2 2004
PATENT & TRADEMARK OFFICE

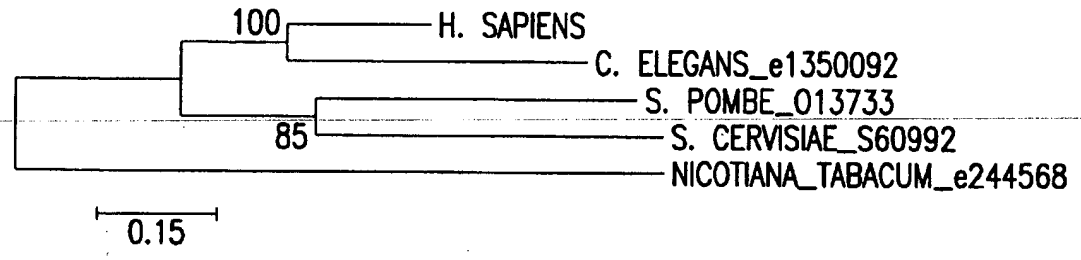


FIG. 14B

OIPE
AUG 0 2 2004
TRADEMARK OFFICE

BASE COUNT 405 a 545 c 493 g 278 t 6 others
ORIGIN

```
   1 cagccgaagc amgcaaaaat tcttccagga gctgagcaag agcctggacg cattccctga
  61 ggayttctgt cggcacaagg tgctgcccca gctgctgacc gccttcgagt tcggcaatgc
 121 tggggccgtt gtcctcacgc ccctcttcaa ggtgggcaag ttcctgagcg ctgaggagta
 181 tcagcagaag atcatccctg tggtggtcaa gatgttctca tccactgacc gggccatgcg
 241 catccgcctc ctgcagcaga tggagcagtt catccagtac cttgacgagc caacagtcaa
 301 cacccagatc ttcccccacg tcgtacatgg cttcctggac accaaccctg ccatccggga
 361 gcagacggtc aagtccatgc tgctcctggc cccaaagctg aacgaggcca acctcaatgt
 421 ggagctgatg aagcactttg cacggctaca ggccaaggat gaacagggcc ccatccgctg
 481 caacaccaca gtctgcctgg gcaaaatcgg ctcctacctc agtgctagca ccagacacag
 541 ggtccttacc tctgccttca gccgagccac tagggacccg tttgcaccgt cccgggttgc
 601 gggtgtcctg ggctttgctg ccacccacaa cctctactca atgaacgact gtgcccagaa
 661 gatcctgcct gtgctctgcg gtctcactgt agatcctgag aaatccgtgc gagaccaggc
 721 cttcaaggcm wttcggagct tcctgtccaa attggagtct gtgtcggagg acccgaccca
 781 gctggaggaa gtggagaagg atgtccatgc agcctccagc cctggcatgg gaggagccgc
 841 agctagctgg gcaggctggg cgtgaccggg gtctcctcac tcacctccaa gctgatccgt
 901 tcgcacccaa ccactgcccc aacagaaacc aacattcccc aaagacccac gcctgaagga
 961 gttcctgccc cagcccccac ccctgttcct gccaccccta caacctcagg ccactgggag
1021 acgcaggagg aggacaagga cacagcagag gacagcagca ctgctgacag atgggacgac
1081 gaagactggg gcagcctgga gcaggaggcc gagtctgtgc tggcccagca ggacgactgg
1141 agcaccgggg gccaagtgag ccgtgctagt caggtcagca actccgacca caaatcctcc
1201 aaatccccag agtccgactg gagcagctgg gaarctgagg gctcctggga acagggctgg
1261 caggagccaa gctcccagga gccacctyct gacggtacac ggctggccag cgagtataac
1321 tggggtggcc cagagtccag cgacaagggc gaccccttcg ctaccctgtc tgcacgtccc
1381 agcacccagc cgaggccaga ctcttggggt gaggacaact gggagggcct cgagactgac
1441 agtcgacagg tcaaggctga gctggcccgg aagaagcgcg aggagcggcg gcgggagatg
1501 gaggccaaac gcgccgagag gaaggtgcca agggccccat gaagctggga gcccggaagc
1561 tggactgaac cgtggcggtg gcccttcccg gctgcggaga gcccgcccca cagatgtatt
1621 tattgtacaa accatgtgag cccggccgcc cagccaggcc atctcacgtg tacataatca
1681 gagccacaat aaattctatt tcacaaaaaa aaaaaaaaaa aaaaaaa
//
```

FIG. 14C

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```
          5         10        15        20        25        30
 1  S R S X Q K F F Q E L S K S L D A F P E D F C R H K V L P Q
31  L L T A F E F G N A G A V V L T P L F K V G K F L S A E E Y
61  Q Q K I I P V V V K M F S S T D R A M R I R L L Q Q M E Q F
91  I Q Y L D E P T V N T Q I F P H V V H G F L D T N P A I R E
121 Q T V K S M L L L A P K L N E A N L N V E L M K H F A R L Q
151 A K D E Q G P I R C N T T V C L G K I G S Y L S A S T R H R
181 V L T S A F S R A T R D P F A P S R V A G V L G F A A T H N
211 L Y S M N D C A Q K I L P V L C G L T V D P E K S V R D Q A
241 F K A X R S F L S K L E S V S E D P T Q L E E V E K D V H A
271 A S S P G M G G A A A S W A G W A
```

ID11

FIG. 14D

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```
>sp|P15533|RPT1_MOUSE DOWN REGULATORY PROTEIN OF INTERLEUKIN 2 RECEPTOR
(J03776) rpt-1r [Mus musculus] Length = 353

Score = 92.0 bits (237), Expect = 6e-20

Query 194  VMELLEEDLTCPICCSLFDDPRVLPCSHNFCKKCLEGILEGSVRNSMWRPAPFKCPTCRK  373
           V+E+++E++TCPIC  L  +P    C+H+FC+ C+    E S RN+         CP CR
Sbjct 5    VLEMIKEEVTCPICLELLKEPVSADCNHSFCRACITLNYE-SNRNT---DGKGNCPVCRV  60

Query 374  ETSATGINSLQVNYSLKGIVEKYNKIKISP----KMPVCKGHMGQPLNIFCLTDMQLICG  541
                    +L+ N  +  IVE+    K  P    K+ +C  H G+ L +FC   DM +IC
Sbjct 61   PYP---FGNLRPNLHVANIVERLKGFKSIPEEEQKVNICAQH-GEKLRLFCRKDMMVICW  116

Query 542  ICATRGEHTKHVFCSIEDAYAQERDAFESLFQSF-------ETWRRGDALSRLDTMETSK  700
           +C    EH  H    IE+   + ++  +             + W+    L R+D
Sbjct 117  LCERSQEHRGHQTALIEEVDQEYKEKLQGALWKLMKKAKICDEWQDDLQLQRVDW-----  171

Query 701  RKSLQLMTKDSDKVKEFFEKLQHTLDQKKNEILSDFETMKLAVMQAYDPEINKL  862
              +Q+   + + V+  F+ L+  LD K+NE L   +  K  VM+  +   N+L
Sbjct 172  ENQIQI---NVENVQRQFKGLRDLLDSKENEELQKLKKEKKEVMEKLEESENEL  222

Homology covers ring finger, B-box and the beginning of coiled coil domain
in the CLL ring finger protein
```

FIG. 15

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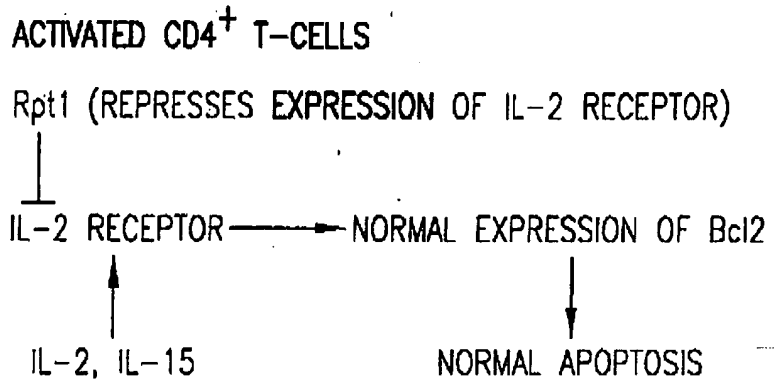

FIG. 16A

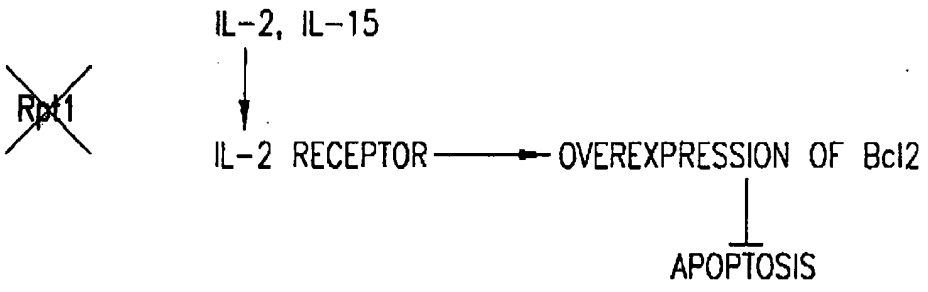

FIG. 16B

O!PE
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TBLASTN 2.0.8 [Jan-05-1999]

Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David L. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25.3389-3402.

Query= gi |2137498|Mad3m
(205 letters)

gb|AA278224|AA278224 zs77e05.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:703520 5' similar to TR:G1184157 G1184157 MAX-INTERACTING TRANSCRIPTIONAL REPRESSOR. ;
Length = 430

Score = 209 bits (526), Expect = 1e-53
Identities = 104/124 (83%), Positives = 116/124 (92%), Gaps = 1/124 (0%)
Frame = +2

```
Query: 1    MEPVASNIQVLLQAAEFLERREREAEHGYASLCPHHSPGTVCRRRKPPLQAPGALNSGRS  60     ID14
             MEP+ASNIQVLLQAAEFLERREREAEHGYASLCPH SPG + RR+K P QAPGA +SGRS        ID15
Sbjct: 56   MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRS  235    ID16

Query: 61   VHNELEKRRRAQLKRCLEQLRQQMPLGVDCTRYTTLSLL-RARVHIQKLEEQEQQARRLK  119
             VHNELEKRRRAQLKRCLE+L+QQMPLG DC RYTTLSLL RAR+HIQKLE+QEQ+AR+LK
Sbjct: 236  VHNELEKRRRAQLKRCLERLKQQMPLGGDCARYTTLSLLRRARMHIQKLEDQEQRARQLK  415

Query: 120  EKLRS 124
             E+LR+
Sbjct: 416  ERLRT 430
```

dbj|C02407|C02407 HUMGS0012279, Human Gene Signature, 3'-directed cDNA sequence.
Length = 348

Score = 97.5 bits (239), Expect = 6e-20
Identities = 51/63 (80%), Positives = 56/63 (87%)
Frame = +3

```
Query: 125 KQQSLQQQLEQLQGLPGARERERLRADSLDSSGLSSERSDSDQEDLEVDVENLVFGTETE  184     ID17
           KQQSLQ+   QL+GL GA ERERLRADSLDSSGLSSERSDSDQE+LEVDVE+LVFG E E        ID18
Sbjct: 45  KQQSLQRXWMQLRGLAGAAERERLRADSLDSSGLSSERSDSDQEELEVDVESLVFGGEAE  224     ID19

Query: 185 LLQ 187
           LL+
Sbjct: 225 LLR 233
```

FIG. 17A

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```
BASE COUNT 130 a    234 c    258 g    106 t      5 others
ORIGIN
  1  cagccgcttg ctccggccgg caccctaggc cgcagtccgc caggctgtcg ccgacatgga
 61  acccttggcc agcaacatcc aggtcctgct gcaggcggcc gagttcctgg agcgccgtga
121  gagagaggcc gagcatggtt atgcgtccct gtgcccgcat cgcagtccag gccccatcca
181  caggaggaag aagcgacccc cccaggctcc tggcgcgcag gacagcgggc ggtcagtgca
241  caatgaactg gagaagcgca ggagggccca gttgaagcgg tgcctggagc ggctgaagca
301  gcagatgccc ctgggcggcg actgtgcccg gtacaccacg ctgagcctgc tgcgccgtgc
361  caggatgcac atccagaagc tggaggatca ggagcagcgg gcccgacagc tcaaggagag
421  gctgcgcaca aagcagcaga gcctgcagcg gcantggatg cagctccggg ggctggcagg
481  ngcggccgag cgggagcgnc tgcgggcgga cagtctggac tcctcaggcc tctcctctga
541  gcgctcagac tcagaccaag aggagctgga ggtggatgtg gagagcctgg tgtttggggg
601  tgaggccgag ctgctgcggg gcttcgtcgc cggccaggag cacagctact cgcacgtcgg
661  cggcgcctgg ctatgatgtt cctcacccan ggcgggcctc tgccctctta ctcgttgccc
721  aagcccactt tnc
```

FIG.17B

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>*Mad*3b(Putative)
MEPLASNIQVLLQAAEFLERREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRSVHNELEKRRRAQLK
RCLERLKQQMPLGGDCARYTTLSLLRRARMHIQKLEDQEQRARQLKERLRTKQQSLQRXWMQLRGLAGAAERER ID27
LRADSLDSSGLSSERSDSDQEELEVDVESLVFGGEAELLRGFVAGQEHSYSHVGGAWL

FIG. 17C

```
gi|25Ø6888|MADe   MATAVGHNIQLLLEAADYLERREREAEHGYASMLPYS-KDADAFKRRNKPKKNST--SSRSTHNEMEKNRRAHLRLCLEKLKGLVPLGPESSRHTTLSLL ID21
gi|729978|MADh    MAAAYRMNIQMLLEAADYLERREREAEHGYASMLPYNNKDRDALKRRNKSKKNNS--SSRSTHNEMEKNRRAHLRLCLEKLLGLVPLGPESSRHTTLSLL 22
gi|2792362|Mad4h  ---MELNSLLILLEAAEYLERRDREAEHGYASVLPFDGDFAREKTKAAGLVRKAP--NNRSSHNELEKHRRAKLRLYLEQLKQLVPLGPDSTRHTTLSLL 23
gi|2137499|Mad4m  ---MELNSLLLLLEAAEYLERRDREAEHGYASMLPFDGDFARKKTKTAGLVRKGP--NNRSSHNELEKHRRAKLRLYLEQLKQLGPLGPDSTRHTTLSLL 24
gi|2137498|Mad3m  -MEPVASNIQVLLQAAEFLERREREAEHGYASLCPHHSPGTVCRRRKPPLQAPGALNSGRSVHNELEKRRRAQLKRCLEQLRQQMPLGVDCTRYTTLSLL 25
Mad3h Putative    -MEPLASNIQVLLQAAEFLFRREREAEHGYASLCPHRSPGPIHRRKKRPPQAPGAQDSGRSVHNELEKRRRAQLKRCLERLKQQMPLGGDCARYTTLSLL 26

gi|25Ø6888|MADe   TKAKLHIKKLEDCDRKAVHQIDQLQREQRHLKRRLEKLGAERTR-------MDSVG-SVVSSERSDSDREELDVDVDVDVDVDVEGTDYLPGDLGWSSS-
gi|729978|MADh    TKAKLHIKKLEDCDRKAVHQIDQLQREQRHLKRQLEKLGIERIR-------MDSIG-STVSSERSDSDRE--------EIDVDVESTDYLTGDLDWSSSS
gi|2792362|Mad4h  KRAKVHIKKLEEQQRRALSIKEQLQQEHRFLKRRLEQLSVQSVER----VRTDSTG-SAVSTD--DSEQE-----------VDIEGMEFGPGELDSVGS-
gi|2137499|Mad4m  K-AKMHIKKLEEQQRRALSIKEQLQREHRFLKRRLEQLSVQSVR-----VRTDSTG-SAVSTD--DSEQE-----------VDIEGMEFGPGELDSAGS-
gi|2137498|Mad3m  R-ARVHIQKLEEQEQQARRLKEKLRSKQQSLQQQLEQLQGLPGARERPRLRADSLDSSGLSSERSDSDQE--------DLSVDVENLVFG-TETELLQSF
Mad3h Putative    RRARMHIQKLEDQEQRARQLKERLRTKQQSLQRXWMQLRGLAGAAERERLRADSLDSSGLSSERSDSDQE--------ELEVDVESLVFG-GEAELLRGF

gi|25Ø6888|MADe   VSDSDERGSMQSLG-SDEGYSSATVKRAKLQQGHKAGLGL
gi|729978|MADh    VSDSDERGSMQSLG-SDEGYSSTSIKRIKLQQSHKACLGL
gi|2792362|Mad4h  SSDADDHYSLQSGTGGDSGFGPHCRRLGRPALS-------
gi|2137499|Mad4m  SSDADDHYSLQSSGCSDSSYGHPCRRPGCPGLS-------
gi|2137498|Mad3m  SAGREHSYSHSTCAWL-----------------------
Mad3h Putative    VAGQEHSYSHVGGAWL-----------------------
```

FIG. 17D

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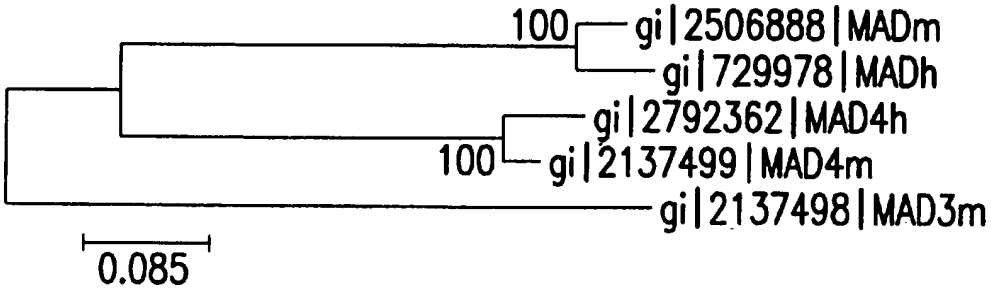

FIG. 18A

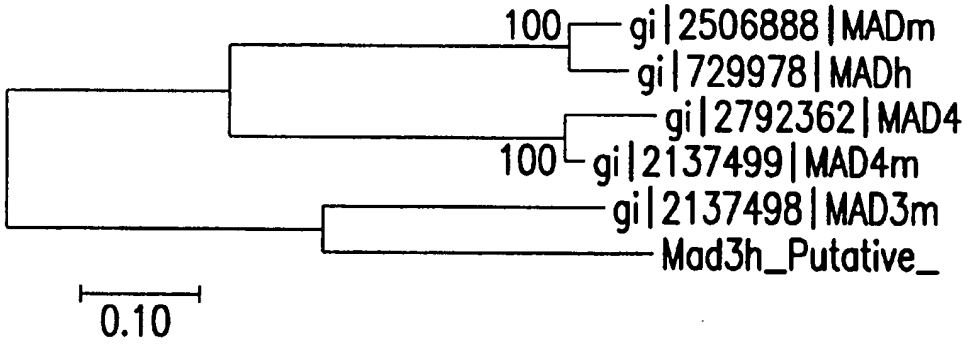

FIG. 18B